

## CONCLUSION

Applicants have attached a check for the additional added claims in the amount of \$54. Should any additional fees or surcharges be deemed necessary, the Examiner has authorization to charge such fees or credit any overpayment to Deposit Account No. 23-3000.

The Examiner is invited to telephone the undersigned attorney if there are any questions.

Respectfully submitted,

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE SPECIFICATION**

Amend the paragraph beginning at Page 1, line 15, to read as follows:

Phototherapy has been in existence for many centuries and has been used to treat various skin surface ailments. As early as 1400 B.C. in India, plant extracts (psoralens), in combination with sunlight, were used to treat vitiligo. In 1903, Von Tappeiner and Jeshirek[,] used eosin as a photosensitizer for treating skin cancer, lupus of the skin, and condylomata of female genitalia. Over the years, the combination of psoralens and ultraviolet A (low-energy) radiation has been used to treat a wide variety of dermatological diseases including psoriasis, parapsoriasis, cutaneous T-cell lymphoma, eczema, vitiligo, areata, and neonatal bilirubinemia. Although the potential of cancer phototherapy has been recognized since the early 1900's, systematic studies to demonstrate safety and efficacy began only in 1967 with the treatment of breast carcinoma. In 1975, Dougherty et al. conclusively established that long-term cure is possible with photodynamic therapy (PDT). Currently, phototherapeutic methods are also being investigated for the treatment of some cardiovascular disorders such as atherosclerosis and vascular restenosis, for the treatment of rheumatoid arthritis, and for the treatment of some inflammatory diseases such as Chron's disease.

Replace the paragraph beginning at Page 6, line 20, to read as follows:

The present invention discloses novel, organic azide derivatives and their bioconjugates for phototherapy of tumors and other lesions. More specifically, the present invention discloses organic azide compounds having the formula:



$N_3$  is the azide moiety that produces nitrene upon photoactivation. Ar is a chromophore that undergoes sensitization. This chromophore (Ar) is an aromatic or a heteroaromatic radical derived from the group consisting of benzenes, polyfluorobenzenes, naphthalenes, naphthoquinones, anthracenes, anthraquinones, phenanthrenes, tetracenes, naphthacenediones, pyridines, quinolines, isoquinolines, indoles, isoindoles, pyrroles, imidazoles, pyrazoles, pyrazines, purines, benzimidazoles, benzofurans, dibenzofurans, carbazoles, acridines, acridones, phenanthridines, thiophenes, benzothiophenes, dibenzothiophenes, xanthenes, xanthones, flavones, coumarins, and anthacylines. E is an epitope and is selected from the group consisting of somatostatin receptor binding molecules, ST receptor binding molecules, neurotensin receptor binding molecules, bombesin receptor binding molecules, CCK receptor binding molecules, steroid receptor binding molecules, and carbohydrate receptor binding molecules. L is a linker between the chromophore and the

epitope and is selected from the group consisting of  $-(CH_2)_a-$ ,  $-(CH_2)_bCONR^1-$ ,  $-N(R^2)CO(CH_2)_c-$ ,  $-OCO(CH_2)_d-$ ,  $-(CH_2)_eCO_2-$ ,  $-OCONH-$ ,  $-OCO_2-$ ,  $-HNCONH-$ ,  $-HNCSNH-$ ,  $-HNNHCO-$ ,  $-OSO_2-$ ,  $-NR^3(CH_2)_eCONR^4-$ ,  $-CONR^5(CH_2)_fNR^6CO-$ , and  $-NR^7CO(CH_2)_gCONR^8-$ . X is either a single bond or is selected from the group consisting of  $-(CH_2)_h-$ ,  $-OCO-$ ,  $-HNCO-$ ,  $-(CH_2)_iCO-$ , and  $-(CH_2)_jOCO-$ . R<sup>1</sup> to R<sup>8</sup> are independently selected from the group consisting of hydrogen, C1-C10 alkyl, -OH, C1-C10 polyhydroxyalkyl, C1-C10 alkoxy, C1-C10 alkoxyalkyl, -SO<sub>3</sub>H, -(CH<sub>2</sub>)<sub>k</sub>CO<sub>2</sub>H, and -(CH<sub>2</sub>)<sub>l</sub>NR<sup>9</sup>R<sup>10</sup>. R<sup>9</sup> and R<sup>10</sup> are independently selected from the group consisting of hydrogen, C1-C10 alkyl, C5-C10 aryl, and C1-C10 polyhydroxyalkyl. [And] a to I independently range from 0 to 10.

Replace the paragraph beginning at Page 12, line 21, to read as follows:

In a second embodiment, azides according to the present invention have the general formula shown above wherein Ar is selected from the group consisting of tetrafluorobenzenes, phenanthridines, xanthones, anthraquinones, acridines, and acridones; E [a] selected from the group consisting of octreotide and octreotate peptides, heat-sensitive bacterioendotoxin receptor binding peptides, carcinoembryonic antigen antibody (anti-CEA), bombesin receptor binding peptide, neuropeptides, receptor binding peptide, cholecystekinin receptor binding peptide, and estrogen steroids; L is selected from the group consisting of -HNCO-, -

$\text{CONR}^1$ - $\text{-HNCSNH}$ - $\text{-HNNHCO}$ - $\text{-}(\text{CH}_2)_a\text{CONR}^1$ - $\text{-CONR}^1(\text{CH}_2)_a\text{NR}^2\text{CO}$ -; and  $R^1$  and  $R^2$  are independently selected from the group consisting of hydrogen, C1-C10 alkyl, C1-C5 polyhydroxyalkyl; and  $a$ ,  $b$ , and  $c$  independently range from 0 to 6.

### **IN THE CLAIMS**

11. (AMENDED) A method of performing a phototherapeutic procedure which comprises:

(a) administering an effective amount of an organic azide photosensitizer having the formula



wherein Ar is an aromatic or a heteroaromatic radical derived from the group consisting of benzenes, polyfluorobenzenes, naphthalenes, naphthoquinones, anthracenes, anthraquinones, phenanthrenes, tetracenes, naphthacenediones, pyridines, quinolines, isoquinolines, indoles, isoindoles, pyrroles, imidazoles, pyrazoles, pyrazines, purines, benzimidazoles, benzofurans, dibenzofurans, carbazoles, acridines, acridones, phenanthridines, thiophenes, benzothiophenes, dibenzothiophenes, xanthenes, xanthones, flavones, coumarins, and anthacylines; E is a hydrogen atom or is selected from the group consisting of somatostatin receptor binding molecules, ST receptor binding molecules, neurotensin receptor binding molecules, bombesin receptor binding molecules, CCK receptor binding molecules, steroid receptor binding molecules, and

carbohydrate receptor binding molecules; L is selected from the group consisting of -  
(CH<sub>2</sub>)<sub>a</sub>-,-(CH<sub>2</sub>)<sub>b</sub>CONR<sup>1</sup>-,-N(R<sup>2</sup>)CO(CH<sub>2</sub>)<sub>c</sub>-,-OCO(CH<sub>2</sub>)<sub>d</sub>-,-(CH<sub>2</sub>)<sub>e</sub>CO<sub>2</sub>-,-OCONH-,-  
OCO<sub>2</sub>-,-HNCONH-,-HNCSNH-,-HNNHCO-,-OSO<sub>2</sub>-,-NR<sup>3</sup>(CH<sub>2</sub>)<sub>e</sub>CONR<sup>4</sup>-,-  
CONR<sup>5</sup>(CH<sub>2</sub>)<sub>f</sub>NR<sup>6</sup>CO-, and -NR<sup>7</sup>CO(CH<sub>2</sub>)<sub>g</sub>CONR<sup>8</sup>-; X is either a single bond or is  
selected from the group consisting of -(CH<sub>2</sub>)<sub>h</sub>-,-OCO-, -HNCO-, -(CH<sub>2</sub>)<sub>i</sub>CO-, and -  
(CH<sub>2</sub>)<sub>j</sub>OCO-; R<sup>1</sup> to R<sup>8</sup> are independently selected from the group consisting of hydrogen,  
C1-C10 alkyl, -OH, C1-C10 polyhydroxyalkyl, C1-C10 alkoxy, C1-C10 alkoxyalkyl, -  
SO<sub>3</sub>H, -(CH<sub>2</sub>)<sub>k</sub>CO<sub>2</sub>H, and -(CH<sub>2</sub>)<sub>l</sub>NR<sup>9</sup>R<sup>10</sup>; R<sup>9</sup> and R<sup>10</sup> are independently selected from the  
group consisting of hydrogen, C1-C10 alkyl, C5-C10 aryl, and C1-C10 polyhydroxyalkyl;  
and subscripts a to l independently range from 0 to 10; and

- (b) [allowing said photosensitizer to accumulate in target tissue; and
- (c)] exposing said target tissues with the light of wavelength between 300  
and 950 nm with sufficient power and fluence rate to perform the phototherapeutic  
procedure.

New claims 21 through 27 are added.